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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,469	01/25/2001	Tony Kouzarides	620-128	8432

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EXAMINER

.KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 04/22/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/744,469

Applicant(s)

KOUZARIDES, TONY

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-10 and 12-18 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 12-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2, 4-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☒ Interview Summary (PTO-413) Paper No(s). 15.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Status of the Claims

1. Claims 1, 2, 4-10 and 12-18 are pending.

Applicants' amendment filed on February 7, 2003 (Paper No. 14) is acknowledged, and applicants' response has been fully considered. Claims 2, 4, 5 and 8-10 have been amended, and claims 3 and 11 have been cancelled. Claims 1 and 12-18 are non-elected inventions, thus withdrawn from consideration. Therefore, claims 2 and 4-10 are examined.

Objection Withdrawn

2. The previous objection of the specification regarding without citing "SEQ ID NO:" at page 3, is withdrawn in view of applicants' amendment, which has been entered in Paper No. 4.
3. The previous objection of claims 2-11 is withdrawn in view of applicants' amendment to the claim in Paper No. 14.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

4. The previous rejection of claims 2-11, under 35 U.S.C.112, second paragraph, regarding claim 2 lacking essential steps; claims 10 and 11 containing non-elected invention; and the term "Importin α activity", "and/or", "determining interaction between the first and second substances", "a region Importin α ", "a said region", "determining interaction between said substance and the test compound" or "at least one additional component", is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 5-7 and 9 in Paper No. 14.

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Claim Objection

5. Claim 4 is objected to because of the term "said interaction the absence of test compound" in step (c). Inserting the word "in" between "interaction" and "the absence" is suggested.
6. Claims 6-8 are objected to because of the use of the term "A method according to claim 5". Claims 6-8 are dependent from claim 5, thus the term "The method according to claim 5" should be used.
7. Claim 10 is objected to because the claim is dependent from a non-elected claim, claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 4 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying an agent which inhibits the binding of CBP to Importin α , comprising (a) contacting CBP or a specific CBP peptide (residues 1078-1785), Importin α or N-terminal peptide of Importin α (residues 1-95), and a test compound, (b) determining the binding between CBP or the CBP peptide and Importin α or the Importin α peptide, and (c) comparing the binding in the presence and absence of the test compound, where inhibition of CBP and Importin α binding identifies the test compound as an inhibitory modulator of CBP and Importin α binding; or, a method for identifying an agent which binds to a specific region of CBP or a specific region of Importin α , wherein the region of

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CBP binds to the region of Importin α , where the acetylation of Importin α occurs, an agent which binds to the region of CBP or the region of Importin α being an inhibitor of CBP and Importin α binding, comprising (a) contacting CBP, CBP peptide (residues 1078-1785), Importin α , or Importin α peptide (residues 1-95) to a test compound, (b) determining the binding between CBP, the CBP peptide, Importin α or Importin α peptide, and a test compound, does not reasonably provide enablement for a method for identifying an agent which modulates interaction between CBP and Importin α , comprising the steps of (a) contacting a CBP peptide, an Importin α peptide, and a test compound, (b) determining the interaction between the CBP peptide and the Importin α peptide, and (c) comparing the interaction in the presence and absence of the test compound, where the CBP peptide or the Importin α peptide is not defined; or, a method for identifying an agent which interacts with a region of CBP or a region of Importin α , wherein the region of CBP interacts with Importin α , and the region of Importin α interacts with CBP, where the region of CBP or the region of Importin α is not defined, the agent which interacts with the region of CBP or the region of Importin α being a modulator of interaction between CBP and Importin α , comprising (a) contacting a CBP peptide or an Importin α peptide to a test compound, (b) determining the interaction between the CBP peptide or the Importin α peptide and a test compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

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Claims 4 and 9 are directed to a method for identifying an agent which modulates interaction between CBP and Importin α , or a method for identifying an agent which interacts with a region of CBP or a region of Importin α . The specification, however, only discloses cursory conclusions without data supporting the findings, which states that methods of obtaining agents able to modulate interaction between CBP and Importin α include methods wherein a suitable end-point is used to assess interaction in the presence and absence of a test compound, assay systems are used to determine CBP acetylase activity, CBP interaction with Importin α , and/or acetylation of Importin α by other acetylases, e.g., activators or inhibitors of CBP-associated acetylase activity able to acetylate Importin α may be identified (pages 4-5). There are no indicia that the present application enables the full scope in view of a method for identifying an agent which modulates interaction between CBP and Importin α as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claim is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the agent identified as a modulator for interaction of CBP and Importin α , the CBP peptide or the

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Importin α peptide used in the assay, and the region of CBP or the region of Importin α interacting with the agent identified, which are not adequately described or demonstrated in the specification.

(2). The absence of working examples:

There are no working examples indicating the claimed methods in association with the variants, e.g., the agent identified by the claimed method as an activator for the interaction between CBP and Importin α , the CBP peptide other than the CBP HAT domain (residues 1078-1785), or the Importin α peptide other than the N-terminal fragment of Importin α .

(3). The state of the prior art and relative skill of those in the art:

The prior art in the specification (pages 1- 3) indicates CBP identified as a histone acetyltransferase has specificity for distinct lysines within the histone, and Importin α is a shuttling NLS (nuclear localization signal) receptor which mediates the import into the nucleus of NLS-containing proteins. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on identities of the activators which modulate the interaction between CBP and Importin α , the CBP peptide other than HAT domain, or the Importin α peptide other than the acetylated region of Importin α , to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method for identifying an agent which modulates interaction between CBP and Importin α using the CBP peptide and Importin α peptide, or a method for identifying an agent which interacts with a region of CBP or a region of Importin α . However,

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the specification does not identify various CBP peptides or Importin α peptides except for the CBP HAT domain or the N-terminal fragment of Importin α , nor indicates various interaction regions between CBP and Importin α besides the acetylated region of Importin α , the invention is highly unpredictable regarding the agent identified as a modulator for the interaction between CBP and Importin α .

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for identifying an agent which modulates interaction between CBP and Importin α using the CBP peptide and Importin α peptide, or a method for identifying an agent which interacts with a region of CBP or a region of Importin α . The specification indicates the CBP HAT domain acetylates Importin α at its N-terminus, and the acetylation residues (Lys 18, Lys20 and Lys 22) of Importin α are identified in the region of residues 17-23, which coincides with the Importin β -binding region of Importin α , and the binding of Importin β is need for nuclear import (pages 58-60). The specification also indicates acetylation of importin α by CBP in vitro stimulates Importin α binding to Importin β .

However, the specification has not demonstrated the use of any CBP peptide other than CBP HAT domain, or any Importin α peptide other than its N-terminal fragment to identify an agent which is a modulator of the interaction of CBP and Importin α . Furthermore, the specification has not identified any region of Importin α besides the acetylated region would interact with CBP, or any agent which is an activator for the interaction of CBP and Importin α . There is no

working example demonstrating the claimed method. Since the specification fails to provide sufficient teachings on the identities of various CBP peptides or Importin α peptides used in the assay; various interaction regions of CBP and Importin α , it is necessary to carry out further experimentation to identify an agent by the claimed method and to assess its effects on modulating the interaction between CBP and Importin α .

(6). Nature of the Invention

The scope of the claims encompasses a method of identifying an agent which modulates interaction between CBP and Importin α , however, the specification has not demonstrated the agent identified by the method modulates the interaction between CBP and Importin α . Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broader than the enabling disclosure, the working examples do not demonstrate the outcome of the method, which is unpredictable, and the teaching in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the agent identified by the claimed method on modulation of the interaction between CBP and Importin α .

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 2 and 4-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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10. Claims 2 and 4-10 are indefinite because of the use of term "CBP". The "CBP" renders the claim indefinite, it is unclear what the term "CBP" means. A full spelled out word should be indicated at the first occurrence in each independent claim. Claims 6-8 and 10 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

In response, applicant cites the term "CREB binding protein" for "CBP". The response is not persuasive because it is not clear what "CREB" represents. Use of "cAMP-response element binding protein" for "CBP".

11. Claim 4 is indefinite because of the use of term "CBP polypeptide or peptide" or "Importin α polypeptide or peptide". The "CBP polypeptide or peptide" or "Importin α polypeptide or peptide" renders the claim indefinite, it is unclear what "CBP polypeptide or peptide" or "Importin α polypeptide or peptide" is, and how different the peptide is as compared to the parent compound, CBP or Importin α .

12. Claims 5-8 are indefinite because the claim cites a method for identifying an agent which affects the activities of Importin α by determining its effect on CBP transferase activity without indicating the acetylation of Importin α by CBP and the step of determining the effect of the agent on the activities of Importin α . Claims 6-8 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

In response, applicants indicate claim 5 has been amended to indicate the effect of an agent on the ability of Importin α to bind Importin β , to translocate into the nucleus, or to import

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a cargo protein is determined through the determination of the effect of the agent on CBP transferase activity, the instant application shows CBP acetyltransferase activity modulates the activity of Importin α , and the effect of such an agent can be confirmed by measuring Importin α activity using the techniques available in the art and are cited in the specification. The response has been fully considered, however, the argument is not persuasive because the claim does not indicate the acetylation of Importin α by CBP and determination of the effect of agents on Importin α activities, without including such steps, it is not clear whether the agent identified by the method actually affect the Importin α activities as indicated in the section above.

13. Claim 9 is indefinite because of the use of term "a region of CBP" or "a region of Importin α ". The "a region of CBP" or "a region of Importin α " renders the claim indefinite, it is unclear which segment of CBP is "a region of CBP", or which segment of Importin α is "a region of Importin α ".

Conclusion

14. No claims are allowed.

A proposed Examiner's Amendment has been faxed to the applicant on April 15, 2003, however, applicant declines.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the

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organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. *CMK*
Patent Examiner

April 18, 2003

Christopher S. F. Low

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